

REMARKS

Claims 11, 13-28 and 32 are pending in the application, and stand rejected. Claim 11 has been amended to make clear that an active platinum compound, a sterol, and one or more phosphatidylcholines are combined in step (a); the phosphitidylcholines are DPPC, DSPC, or mixtures thereof; and that the mixture in step (b) is the resultant mixture from step (a). Support for the amendment to claim 11 can be found throughout the application, such as in paragraph [27] on pages 6 and 7. Claims 1-10 and 29-31, which had been withdrawn, have been canceled.

Importantly, the claim amendments and cancelations are made solely to expedite the prosecution of the above-identified application. Further, the Applicants expressly reserve the right to prosecute the original claims or similar claims in one or more applications entitled to the priority date of the instant application. 35 U.S.C. §§ 120, 121.

RESPONSE TO REJECTIONS UNDER 35 U.S.C. § 103*Abra in view of Ye*

The Examiner has rejected claims 12, 16, 19-23 as being obvious over Abra in view of U.S. Patent No. 5,998,899 to Ye et al. ("Ye"). It is surmised that the Examiner intended to reject claim 11 not claim 12, as claim 12 has been canceled. The Examiner notes that "[w]hat is lacking in Abra is the repetition of the heating and cooling." *Office Action* at p. 3. The Examiner further notes that Abra does not teach the use of DPPC. *Id.* According to the Examiner, it would have been obvious "[t]o employ three cooling and heating cycles in the method . . . of Abra . . . since Ye et al teach that three cooling and heating cycles across the phase transition temperature facilitates drug equilibrium across the bilayer membranes." *Office Action* at p. 3. Furthermore, the Examiner asserts that it would have been obvious to use DPPC instead of HSPC taught by Abra. Applicants respectfully traverse.

In order to establish a *prima facie* case of obviousness, the Examiner must determine the scope and content of the prior art, ascertain the differences between the claimed invention and the prior art and resolve the level of ordinary skill in the pertinent art. Once an Examiner has made a

prima facie case of obviousness, secondary considerations, if they are present, must also be considered in an obviousness determination. *See* MPEP § 2145. Rebuttal evidence to a *prima facie* showing may also include evidence that the claimed invention yields unexpectedly improved properties or properties not present in the prior art. Assuming *arguendo* herein that a *prima facie* case of obviousness has been made, Applicants respectfully assert that the unexpectedly improved results disclosed in the instant application establish the nonobviousness of the pending claims.

As noted above, the pending claims have been amended to make clear that the lipid complex-forming lipids are phosphatidylcholines selected from the group consisting of DPPC, DSPC, and mixtures thereof. Percent entrapment and drug to lipid ratios for formulations of DPPC or DSPC with cholesterol and cisplatin are provided in Table 4, on page 10, in the instant application. When three cycles of warming and cooling have occurred, the percent of cisplatin entrapment for DPPC and DSPC increases from 4.3% to 21.3% and 2.5% to 14.5%, respectively. In other words, the claimed method results in a almost 5-fold increase in encapsulation of cisplatin when DPPC is used and an almost 6-fold increase in encapsulation of cisplatin when DSPC is used. Neither Abra nor Ye teach nor suggest that heat and cooling would result in a 5- to 6-fold increase in encapsulation. Therefore, because of the unexpectedness of such a large increase in encapsulation, the Applicants respectfully request the Examiner withdraw the rejection of the pending claims as unpatentable over Abra in view of Ye.

Yamauchi in view of Abra and Ye

The Examiner has rejected claims 11, 13-14, 16-28 and 32-33 as being obvious over U.S. Publication 2002/0182248 to Yamauchi (“Yamauchi”). The Examiner acknowledges that Yamauchi does not teach “the use of cisplatin as the drug and also repeating the steps of changing the temperature in two or more cycles.” *Office Action* at p. 5. The Examiner contends that it would have been obvious to use cisplatin in the method of Yamauchi “since Yamauchi teaches that any drug can be encapsulated and . . . Abra shows the knowledge in the art of encapsulating cisplatin.” *Id.* at p. 6 The Examiner further contends that it would have been obvious “[t]o employ three cooling and heating cycles . . . since Ye et al teach that three cooling and heating cycles across the

phase transition temperature facilitates drug equilibrium across the bilayer membranes.” *Id.* at p. 6. Applicants respectfully traverse.

The Applicants respectfully assert that Yamauchi fails to remedy the deficiencies of Abra and Ye noted above. Specifically, Yamauchi provides no teaching that heat and cooling would result in a 5- to 6-fold increase in encapsulation. Therefore, the Applicants respectfully request the Examiner withdraw the rejection of the pending claims as unpatentable over Yamauchi in view of Abra and Ye.

CONCLUSION

In light of the amendments and remarks set forth above, Applicants submit that the pending claims are in condition for allowance. Reconsideration and timely allowance of the pending claims is respectfully solicited. If a telephone conference would be helpful, the Examiner is invited to call the undersigned at 617-832-1703. Applicants hereby request that any additional fees required for timely consideration of this application be charged to Deposit Account No. **06-1448**, Reference **TRA-006.01**.

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Respectfully submitted,

/ Jacob I. Wasserman /
Jacob I. Wasserman, Ph.D.
Registration No.: 56,929
FOLEY HOAG LLP
155 Seaport Blvd
Boston, Massachusetts 02210
(617) 832-1703
Agent for Applicants